

1                   AN AQUEOUS NON-ALCOHOLIC ORAL RINSE CONTAINING  
'2                   BENZOCAINE AND CARBOMER

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'4           Field of the Invention

5           The instant invention relates to an oral rinse. More specifically, the instant invention  
6 relates to an aqueous non-alcoholic oral rinse that contains benzocaine and carbomer.

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8           Background Art

9           Oral rinse (mouthwash) compositions have been used for many years to prevent  
10 bad breath and eliminate bacteria and other microorganisms responsible for bad breath,  
11 tooth decay, plaque and gum diseases (such as gingivitis and periodontitis). Conventional  
12 oral rinses generally contain high levels of an alcoholic solvent such as ethanol (percentages  
13 may range anywhere from approximately 10% to about 30% by volume). The alcoholic  
14 solvent serves as a disinfectant, a preservative, and as a dispersant for other additives.

15           However, the use of alcohol has a number of undesirable physical effects. Chronic  
16 exposure to alcohol has been found to result in gum "burn." In addition, persons afflicted  
17 with dry-mouth syndrome must avoid alcohol because it removes moisture from the oral  
18 tissues, thereby aggravating the condition. Furthermore, there is a concern that children can  
19 be adversely affected by inadvertently swallowing alcoholic oral rinse compositions.

20           There are also a number of societal concerns that make the use of alcohol  
21 undesirable. For example, persons of certain religious beliefs may not ingest alcohol in any  
22 form. Furthermore, recovering alcoholics are advised to avoid all alcohol containing oral  
23 compositions.

24           Several attempts at formulating non-alcoholic mouthwash compositions can be  
25 found in the prior art. Examples of such compositions include U.S. Patent Nos. 5,817,295;  
26 5,723,106; 5,707,610; 5,560,906; 5,407,664; 5,292,527; and 4,919,918. None of the  
27 disclosed compositions contain benzocaine, a compound used to treat aphthous ulcers.  
28 This is because benzocaine is only slightly soluble in water.

1           Aphthous ulcers, often referred to as canker sores, are characterized by painful  
2           eruptions in the mucous membrane of the mouth. Of unknown etiology, these sores are  
3           covered by a grey/white exudate and surrounded by a reddened area. They range in size  
4           from several millimeters to two centimeters in diameter. The ulcers are limited to oral  
5           mucous membranes not bound to periosteum, e.g., the inner portion of the lip or cheek.  
6           Aphthous ulcers may occur as solitary or multiple lesions. Generally, these ulcers heal  
7           spontaneously in one or two weeks.

8           Therapy for aphthous ulcers and mouth sores generally involves the use of a topical  
9           anesthetic such as benzocaine. Benzocaine can be dispersed in aqueous oral rinses by using  
10          alcoholic solvents such as ethanol. However, benzocaine is only sparingly soluble in water  
11          alone. According to the Merck Index, "One gram dissolves in about 2500 mL water," or  
12          only 0.04% w/v. Prior to this invention, it has not been possible to disperse benzocaine in  
13          an aqueous media (beyond the very low level identified by the Merck) absent the use of  
14          alcoholic solvents. Thus, a non-alcoholic aqueous oral rinse containing effective amounts of  
15          benzocaine to treat ulcers has not been possible.

### 16 17          Summary of the Invention

18          The invention is directed to an aqueous non-alcoholic oral rinse that contains  
19          benzocaine in a sufficient amount to relieve the soreness of aphthous ulcers and similar  
20          mouth sores. It has been discovered that a carbomer can be used to effectively disperse  
21          the benzocaine into a non-alcoholic aqueous solution.

22          The essential ingredients of the composition are benzocaine, carbomer, and water.  
23          However, a neutralizing agent is preferably employed to "over-neutralize" the carbomer, and  
24          thereby generate a transparent solution. In addition, various additives commonly employed  
25          in the oral rinse art may be employed that include preservatives, antibacterial agents,  
26          buffering agents, surfactants, sweetening agents, flavoring agents, humectants, emulsifiers,  
27          and colorants.

**Disclosure of the Invention**

The invention is an aqueous non-alcoholic oral rinse that contains benzocaine in a sufficient amount to relieve the soreness associated with aphthous ulcers and similar mouth sores. By the term "aqueous" it is meant that the predominant solvent in the system is water. By the term "non-alcoholic" it is meant that aliphatic alcoholic solvents such as ethanol are not present in the composition.

The first essential component of the oral rinse composition is benzocaine ( $C_9H_{11}NO_2$ ). Benzocaine is a known anesthetic that is also known as ethyl amino benzoate and p-aminobenzoic acid ethyl ester. Benzocaine is added in an amount above 0.04%, and preferably above 0.07% by weight of the oral rinse. Preferably, benzocaine is employed in "sub-therapeutic levels" - meaning levels below the amount typically used in OTC Drug applications (5% by weight or more). Thus the most preferred range of benzocaine in the oral rinse is between 0.04% and 5% by weight.

The second essential component of the invention is a polyacrylic acid of the type sold by B.F. Goodrich under the tradename Carbopol®. The USP-NF, the British Pharmacopoeia, the United States Adopted Names Council (USAN), and the Cosmetic, Toiletries and Fragrance Association (CTFA), have all adopted the generic (i.e., nonproprietary) name "carbomer" for the Carbopol® polymers. Carbomers fall into the following two categories: (1) homopolymers of acrylic acid crosslinked with allyl sucrose, polyalkyl ethers of divinyl glycol, or allyl pentaerythritol; and (2) similarly crosslinked copolymers of acrylic acid with minor levels (less than 10% by weight) of long chain alkyl acrylate comonomers. A carbomer's acrylic acid content is generally 90% or more, by weight. The preferred acrylic acid monomer used to make a carbomer is the actual compound "acrylic acid." However, other acrylic acids can also be employed, e.g. methacrylic acid and  $C_{1-4}$  alkyl substituted acrylic acid.

The most preferred carbomers include the products Carbopol® ETD™ 2001, Carbopol® ETD™ 2020, and Carbopol® ETD™ 2050. These "easy-to-disperse

1 (ETD™)" carbomers are homopolymers or copolymers of acrylic acid, produced using a  
2 polymerization aid, and crosslinked with a polyalkenyl polyether. Carbopol® ETD™  
3 2001, Carbopol® ETD™ 2020, and Carbopol® ETD™ 2050 are easier to disperse and  
4 mix than other Carbopol® products. The carbomers wet quickly and thereby minimize  
5 lumping. By "wet" it is meant that the white particles of polymer fully disappear (disperse)  
6 into the mixture. The carbomers also hydrate slowly and have a lower viscosity prior to  
7 neutralization than other Carbopol® products. Because of the fast wetting nature and low  
8 viscosity of these carbomers, vigorous agitation is not necessary to disperse them. The fast  
9 wetting nature of these carbomers also aids handling. The most preferred carbomer is  
10 Carbopol® ETD™ 2050.

11 The amount of carbomer used is not particularly limited. However, it is preferred  
12 that the carbomer be used in an amount of no more than 10% by weight and represent  
13 approximately ½ the total weight of the benzocaine employed.

14 It has been discovered that even though benzocaine is only sparingly soluble in  
15 water (0.04% w/v), it can be carried into solution as a neutralizing agent for the carbomer.  
16 The amine portion of the benzocaine acts by neutralizing the carbomer and is carried by the  
17 finely dispersed carbomer into solution, forming a hazy liquid dispersion. An aqueous  
18 solution containing carbomer alone generally has a pH around 1.2. When benzocaine is  
19 added the pH approaches neutrality.

20 Preferably, a small amount of a second neutralizing agent is also added. The  
21 second neutralizing agent is added to "over neutralize" the carbomer - meaning that the pH  
22 is brought to 8.0 or higher. This serves to break down the carbomer's chain length and  
23 reduce its viscosity and, thereby, eliminate the haziness of the dispersion to create a  
24 transparent solution. The most preferred neutralizing agent is triethanolamine. When  
25 neutralizing agents are employed in addition to the benzocaine they are generally present in  
26 an amount ranging from .001 to 3% by weight of the oral rinse. Preferably, the neutralizing  
27 agents are present in the amount of approximately 1.5% by weight of the oral rinse.

1           In addition, a number of conventional oral rinse additives can also be employed.  
2           These additives include preservatives, weak carboxylic acids, antibacterial agents, buffering  
3           agents, surfactants, sweetening agents, and flavoring agents.

4           Preservatives prolong the useful life of the composition. Sodium benzoate is by far  
5           the most preferred preservative. Sodium benzoate is also effective in inhibiting  
6           microorganisms in the formulations described above. An effective concentration range for  
7           sodium benzoate in the composition of the present invention is generally from about 0.05%  
8           to about 0.2% by weight with the most effective level being about 0.1% by weight.  
9           Although sodium benzoate is the most preferred preservative, alternative or additional  
10          preservatives, such as methylparaben may also be used. Generally, the total amount of  
11          preservative employed represents no more than 0.5% by weight of the total oral rinse.

12          Weak carboxylic acids primarily serve as acidulants but also contribute antibacterial  
13          activity to the composition in a synergistic manner with sodium benzoate. Examples of  
14          suitable weak carboxylic acids include citric acid, tartaric acid (D, L, DL, or a mixture  
15          thereof), acetic acid, and benzoic acid. The most preferred carboxylic acid is citric acid.  
16          Preferably, the carboxylic acid should be present in the composition at a concentration of  
17          from 0.01% to about 1.0% by weight of the total with the most desired level being about  
18          0.1%.

19          The synergistic antibacterial properties of sodium benzoate in combination with the  
20          weak acid generally make the presence of additional antibacterial agents unnecessary.  
21          However, additional antibacterial agents may always be added. Antibacterial agents include  
22          phenolic compounds such as  $\beta$ -naphthol, thymol, chlorothymol, amyl-, hexyl-, heptyl- and  
23          octylphenol, hexylresorcinol, hexachlorophene, and phenol; quaternary ammonium  
24          compounds such as quaternary morpholinium alkyl sulfates, cetylpyridinium chloride,  
25          alkyldimethyl benzylammonium chloride, and alkyltrimethyl ammonium halides. In addition,  
26          miscellaneous antibacterial compounds may be employed such as benzoic acid,  
27          formaldehyde, potassium chlorate, tyrothricin, gramicidin, iodine, sodium perborate, and

1 urea peroxide. The amount of antibacterial agent that can be added varies greatly with the  
2 particular antibacterial agent employed and should be evident to one of ordinary skill in the  
3 art. However, this agents, if employed, should never be the predominant non-aqueous  
4 ingredient in the composition.

5 Buffering agents adjust the pH of the final formulation. Generally, the buffering  
6 agent should be capable of bringing the pH to a physiologically acceptable level. Exemplary  
7 buffering agents are alkali metal and alkaline earth metal salts and amine (e.g., ammonium)  
8 salts of weak carboxylic acids. The preferred buffering agents are sodium citrate,  
9 potassium citrate, and sodium acetate. Preferably, the buffering agent should be present in  
10 the composition in a concentration of from about 2.0 to about 5.0% by weight of the total  
11 with the most desired level being about 2.75%.

12 Surfactants may be included in the composition to increasing the spreading  
13 properties of components in the solution, to keep the composition clear, and to prevent the  
14 composition from becoming turbid. Any food grade anionic, cationic or non-ionic  
15 surfactant can be employed. Preferably, the surfactants are nonionic surfactants.  
16 Particularly preferred nonionic surfactants are polysorbates. Polysorbates are  
17 polyoxyethylene fatty acid esters. Polysorbates are obtained by the esterification of sorbitol  
18 with a fatty acid such as stearic acid, lauric acid and palmitic acid under conditions that  
19 cause the splitting out of water from sorbitol, leaving sorbitan. About 20 moles of ethylene  
20 oxide per mole of sorbitol are used in the condensation to effect water solution. Suitable  
21 polysorbates include polysorbate 20 (polyoxyethylene (20) sorbitan monolaurate),  
22 polysorbate 60 (polyoxyethylene (20) sorbitan monostearate), polysorbate 65  
23 (polyoxyethylene (20) sorbitan tristearate), and polysorbate 80 (polyoxyethylene (20)  
24 sorbitan monooleate). The most preferred surfactant is polysorbate 20. When surfactants  
25 are employed, they are generally present in an amount of at least 0.001% and no more than  
26 3%, based on the entire weight of the oral rinse. Preferably, the surfactants represent

1 0.001% to 1% of the oral rinse. Most preferably, the surfactants are 0.001% to 0.5% of  
2 the oral rinse.

3 Sweetening agents may be included in the composition to sweeten the taste of the  
4 composition. While sodium saccharin is the preferred sweetening agent, any food-use  
5 approved natural or artificial sweeteners are contemplated within the scope of the present  
6 invention. These sweeteners are, for example, sorbitol, xylitol, aspartame, and sucrose.  
7 When sodium saccharin is present in the composition it usually represents from 0.001% to  
8 0.25% by weight of the total with the most desired level being about 0.1%. When  
9 employing a sweetening agent other than sodium saccharin any amount required to produce  
10 an equivalent level of sweetening as that obtained with sodium saccharin will suffice.

11 Flavoring agents may also be included in the composition. The flavoring agents can  
12 be selected from cinnamon, cassia, anise, menthol, methyl salicylate, peppermint oil,  
13 spearmint oil, and other known flavor modifiers. Particularly preferred are peppermint,  
14 spearmint oil (both natural and synthetic analog), and a mixture of the two. Flavoring agents  
15 are generally employed in the oral rinse at a concentration of from 0.001% to about 2.0%  
16 by weight of the total. More preferably, the concentration should be from about 0.05% to  
17 about 1.0% with the most desired level being about 0.2%.

18 Other miscellaneous agents may be added including humectants, emulsifiers, and  
19 colorants. A common agent is Amphosol (cocamidopropyl betaine). This chemical is often  
20 used in cleaning formulations and aids the cleaning and foaming properties of the oral rinse.  
21 Generally, Amphosol is employed in an amount no higher than 1.5% by weight and  
22 preferably less than 1.0% by weight of the total composition. Most preferably, Amphosol  
23 represents approximately 0.60% of the composition's weight.

24 The balance of the composition is water. Generally water represents at least 80%  
25 by weight, preferably at least 90% by weight, and most preferably about 94% by weight of  
26 the oral rinse. Water serves as the fluid base for the oral rinse composition.

1           The order of addition of the ingredients is important. One must first disperse the  
2 carbomer in the aqueous media. Then one must add an amount of benzocaine that is  
3 generally equal to two times the w/w% of carbomer. To this dispersion, additional oral  
4 rinse ingredients can be added and dissolved. A transparent oral rinse can be achieved by  
5 the addition of second neutralizing agent such as triethanol amine.

6           The following examples are intended to illustrate, but not limit, the invention:  
7  
8



Example 1 - Alcohol-Free Oral Rinse Containing Benzocaine

A preparation in accordance with the instant invention was prepared from the following components in the following amounts:

Part A (Oil Phase)	
Ingredient	%w/w
Polysorbate 20	0.12
Cocamidopropyl Betaine	0.60
Flavor	0.19
Carbopol ETD 2050	0.04
Benzocaine USP	0.08
Methylparaben NF	0.12
Part B (Water Phase)	
Ingredient	%w/w
Water, Purified	94.10
Sodium Citrate	2.78
Sodium Saccharin	0.09
Sodium Benzoate	0.11
Citric Acid	0.08
Triethanolamine	1.69
Total	100.00

The benzocaine in the above identified composition remains dispersed.

1                   Example 2 - Alcohol-Free Oral Rinse Containing Benzocaine

2                   Similar compositions to that described in Example 1 were made using other non-  
3                   alcoholic organic solvents such as propylene glycol and polyethylene glycol instead of  
4                   carbomer. In addition, compositions containing these organic solvents with emulsifiers such  
5                   as polysorbate, pluronic, and cocamidopropyl betaine were prepared. In all of these  
6                   preparations, only the amount of benzocaine roughly equivalent to that reported by the  
7                   Merck (0.04 w/v) would solubilize. Additions beyond 0.04 g/100 mL water would  
8                   precipitate out of solution in short order.

9                   While the invention has been described in conjunction with the specific  
10                  embodiments outlined above, it is evident that many alternatives, modifications, and  
11                  variations will be apparent to those skilled in the art. In example, some steps may be  
12                  eliminated or performed out of sequence. Accordingly, the preferred embodiments of the  
13                  invention are intended to be illustrative and not limiting. Various changes may be made  
14                  without departing from the spirit and scope of the invention as defined in the claims.